Recapitulation of the embryonic cardiovascular progenitor cell niche.

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Public Summary:
Stem cells often reside in specialized environment call "niches". These niches have a unique structure and signaling proteins. We have studied the niche that exists in the developing heart and have created 3-D bioengineered structures to mimic the unique features of the endogenous niche.

Scientific Abstract:
Stem or progenitor cell populations are often established in unique niche microenvironments that regulate cell fate decisions. Although niches have been shown to be critical for the normal development of several tissues, their role in the cardiovascular system is poorly understood. In this study, we characterized the cardiovascular progenitor cell (CPC) niche in developing human and mouse hearts, identifying signaling pathways and extracellular matrix (ECM) proteins that are crucial for CPC maintenance and expansion. We demonstrate that collagen IV (ColIV) and beta-catenin-dependent signaling are essential for maintaining and expanding undifferentiated CPCs. Since niches are three-dimensional (3D) structures, we investigated the impact of a 3D microenvironment that mimics the in vivo niche ECM. Employing electrospinning technologies, 3D in vitro niche substrates were bioengineered to serve as culture inserts. The three-dimensionality of these structures increased mouse embryonic stem cell differentiation into CPCs when compared to 2D control cultures, which was further enhanced by incorporation of ColIV into the substrates. Inhibiting p300-dependent beta-catenin signals with the small molecule IQ1 facilitated further expansion of CPCs. Our study represents an innovative approach to bioengineer cardiac niches that can serve as unique 3D in vitro systems to facilitate CPC expansion and study CPC biology.